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Express Mail No. EV462737661US

PETITION FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322 FOR PATENT AND TRADEMARK OFFICE ERROR AND UNDER 37 C.F.R. § 1.323 FOR APPLICANT MISTAKE Address to: Assistant Commissioner for Patents Alexandria, VA	Attorney Docket Number	TEIK-004
	First Named Inventor	Jutaro Shudo
	Application Number	10/080,526
	Filing Date	February 21, 2002
	Patent Number	6,761,900 B2
	Issue Date	July 13, 2004
	Title	TOPICAL PATCH PREPARATION CONTAINING A DELAYED HYPERSENSITIVITY INDUCER AND METHODS FOR USING THE SAME

Sir:

Applicants petition under 37 C.F.R. § 1.322 for a Certificate of Correction to correct errors in the claims for the above-identified patent due to Patent and Trademark Office error. In addition, the Applicants petition under 37 C.F.R. § 1.323 for a Certificate of Correction to correct typographical errors in the specification due to Applicant's mistake.

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent. Please make the following corrections to the specification and Claim 1.

Certificate**AUG 13 2004****of Correction**

In the Abstract, line 2, please replace the word "1-dichloro-2,4-dinitrobenzene" with -- 1-chloro-2,4-dinitrobenzene --.

In column 2, line 60, please replace the word "1-dichloro-2,4-dinitrobenzene" with -- 1-chloro-2,4-dinitrobenzene --.

In column 3, line 22, please replace the word "1-dichloro-2,4-dinitrobenzene" with -- 1-chloro-2,4-dinitrobenzene --.

In column 5, line 18, please insert a --) -- after the word "etc" and before the word "and".

In Claim 1, column 11, line 47, please remove the word -- is -- after the word "ionic" and before the word "aluminum".

08/11/2004 MAHMED2 00000045 500815 6761900

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18 AUG 2004

The change of "1-dichloro-2,4-dinitrobenzene" to "1-chloro-2,4-dinitrobenzene" is requested to correct a typographical mistake. The compound name "1-chloro-2,4-dinitrobenzene" is correctly presented in other instances throughout the specification, at for example, Column 4, line 15. Accordingly, the proposed typographical corrections to the specification resulting from Applicants' mistake do not constitute new matter and do not require reexamination.

Enclosed is a copy of the Amendment and Response filed on November 26, 2003, as well as a copy of the Notice of Allowance dated March 2, 2004, which provides the Examiner's Amendment. The two documents show the correct form of Claim 1. Also enclosed, are copies of the relevant pages of the issued patent showing the incorrect language of the specification as well as claim 1.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. § 1.20 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: _____

8.6.04

By: _____

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**UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION**

PATENT NO. : 6,761,900 *B2*
DATED : July 13, 2004
INVENTOR(S) : Jutaro Shudo et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

In the Abstract, line 2, the word "1-dichloro-2,4-dinitrobenzene" should be replaced with -- 1-chloro-2,4-dinitrobenzene --.

In column 2, line 60, the word "1-dichloro-2,4-dinitrobenzene" should be replaced with -- 1-chloro-2,4-dinitrobenzene --.

In column 3, line 22, the word "1-dichloro-2,4-dinitrobenzene" should be replaced with -- 1-chloro-2,4-dinitrobenzene --.

In column 5, line 18, a --) -- should be inserted after the word "etc" and before the word "and".

In Claim 1, column 11, line 47, the word -- is -- after the word "ionic" and before the word "aluminum" should be removed.

MAILING ADDRESS OF SENDER:

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PATENT NO: 6,761,900 *B2*

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18 AUG 2004



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

Complete if Known

Patent Number	6,761,900 <i>B2</i>
Issue Date	July 13, 2004
First Named Inventor	SHUDO, JUTARO
Application Number	10/080,526
Filing Date	February 21, 2002
Attorney Docket No.	TEIK-004

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$100.00)

METHOD OF PAYMENT (check all that apply)☐ Check ☐ Credit Card ☐ Money Order ☐ Other ☐ None☒ Deposit Account:

Deposit Account Number	50-0815
Deposit Account Name	Bozicevic, Field & Francis LLP

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments☒ Charge Any Additional Fee(s) Required under 37 C.F.R. 1.17.☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.**FEE CALCULATION****1. BASIC FILING FEE**

Large Entity Code	Large Entity Fee (\$)	Small Entity Code	Small Entity Fee (\$)	Fee Description
1001	770	2001	385	Utility filing fee
1002	340	2002	170	Design filing fee
1003	530	2003	265	Plant filing fee
1004	770	2004	385	Reissue filing fee
1005	160	2005	80	Provisional filing fee

SUBTOTAL (1)**2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE**

	Extra Claims	Fee from below	Fee Paid
Total Claims	-20** = x		
Indep. Claims	-3** = x		
Multiple Dependent			

Large Entity Code	Large Entity Fee (\$)	Small Entity Code	Small Entity Fee (\$)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) \$

**or number previously paid, if greater; For Reissues, see above.

FEE CALCULATION (continued)**3. ADDITIONAL FEES**

Large Entity Small Entity

Fee Code	Fee (\$)	Fee Code	Fee (\$)	Fee Description
1051	130	2051	65	Surcharge - late filing fee or oath
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet
1053	130	1053	130	Non-English specification
1812	2,520	1812	2,520	For filing a request for ex parte reexamination
1804	920*	1804	920*	Requesting publication of SIR prior to Examination action
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action
1251	110	2251	55	Extension for reply within first month
1252	420	2252	210	Extension for reply within second month
1253	950	2253	475	Extension for reply within third month
1254	1,480	2254	740	Extension for reply within fourth month
1255	2,010	2255	1,005	Extension for reply within fifth month
1401	330	2401	165	Notice of Appeal
1402	330	2402	165	Filing a brief in support of an appeal
1403	290	2403	145	Request for oral hearing
1451	1,510	1451	1,510	Petition to institute a public use proceeding
1452	110	2452	55	Petition to revive - unavoidable
1453	1,330	2453	665	Petition to revive - unintentional
1501	1,330	2501	665	Utility issue fee (or reissue)
1502	480	2502	240	Design issue fee
1503	640	2503	320	Plant issue fee
1406	130	1480	130	Petitions to the Commissioner
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)
1806	180	1806	180	Submission of Information Disclosure Stmt
8021	40	8021	40	Recording each patent assignment per property (times number of properties)
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))
1801	770	2801	385	Request for Continued Examination (RCE)
1802	900	1802	900	Request for expedited examination of a design application

Other fee (specify) Certificate of Correction under 1.323

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$)

100.00

100.00

SUBMITTED BY**Complete (if applicable)**

Name (Print/Type)	Bret E. Field	Registration No. (Attorney/Agent)	37,520	Telephone	(650) 833-7770
Signature				Date	08/06/2004

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

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18 AUG 2004



US006761900B2

(12) **United States Patent**
Shudo et al.

(10) **Patent No.:** US 6,761,900 B2
(45) **Date of Patent:** Jul. 13, 2004

- (54) **TOPICAL PATCH PREPARATION CONTAINING A DELAYED-TYPE HYPERSENSITIVITY INDUCER AND METHODS FOR USING THE SAME**
- (75) Inventors: Jutaro Shudo, San Jose, CA (US);
Ichiro Mori, San Jose, CA (US)
- (73) Assignee: Teikoku Pharma USA, Inc., Campbell, CA (US)
- (*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 10/080,526

(22) Filed: Feb. 21, 2002

(65) **Prior Publication Data**

US 2002/0176886 A1 Nov. 28, 2002

Related U.S. Application Data

(60) Provisional application No. 60/275,213, filed on Mar. 12, 2001.

(51) Int. Cl.⁷ A61F 13/02; A61F 15/16;
A61F 13/00

(52) U.S. Cl. 424/448; 424/449; 424/443

(58) Field of Search 424/448, 449,
424/443

(56) **References Cited**

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Oracion et al. "DNCB treatment of HIV-infected patients leads to beneficial immunologic outcomes, reduced viral load, and improved measures of quality-of-life" *J. Invest Dermatol.* (1998) 110:476.

Stricker et al. Dendritic cells and dinitrochlorobenzene (DNCB): A new treatment approach to AIDS *Immunol Letter* (1991) 29:191-196.

Stricker et al. "Pilot study of topical dinitrochlorobenzene (DNCB) in human immuno deficiency virus infection" *Immunol Letters*, (1993) 36:1-6.

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(List continued on next page.)

Primary Examiner—Gollamudi S. Kishore

Assistant Examiner—Isis Ghali

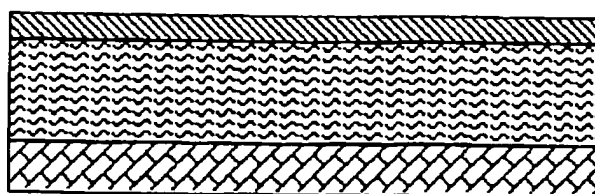
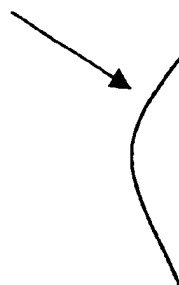
(74) *Attorney, Agent, or Firm*—Bret E. Field; Bozicevic, Field & Francis LLP

(57) **ABSTRACT**

Topical patch preparations that contain a delayed-type hypersensitivity inducer, e.g., 1-dichloro-2,4-dinitrobenzene (DNCB), and methods for using the same are provided. The subject topical patch preparations are made up of an adhesive gel composition that is present on a support, where the adhesive gel composition includes the delayed-type hypersensitivity inducer, a water-soluble polymer gel, water and a water holding agent. In using the subject topical patch preparations, the topical patch preparations are applied to a skin surface of a subject and maintained at the site of application for a period of time sufficient for an effective amount of the delayed-type hypersensitivity inducer to be administered to the subject, where this maintenance period typically does not exceed about 60 minutes. The subject invention finds use in a variety of applications where the administration of a delayed-type hypersensitivity inducer is desired, and is particularly suited for use in the treatment of HIV associated disease conditions, e.g., AIDS.

18 Claims, 3 Drawing Sheets

10



← 16

← 12

← 14

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TOPICAL PATCH PREPARATION CONTAINING A DELAYED-TYPE HYPERSENSITIVITY INDUCER AND METHODS FOR USING THE SAME

CROSS REFERENCE TO RELATED APPLICATIONS

Pursuant to 35 U.S.C. §119(e), this application claims priority to the filing date of the U.S. Provisional Patent Application Serial No. 60/275,213 filed Mar. 12, 2001; the disclosures of which are herein incorporated by reference.

INTRODUCTION

Field of the Invention

The field of this invention is delayed-type hypersensitivity inducing agents.

BACKGROUND OF THE INVENTION

The number of Human Immunodeficiency Virus (HIV) patients worldwide has been increasing rapidly in recent years, and is said to be approximately 33 million (WHO; end of 1998). Against this backdrop, there is a rush to develop a vaccine for HIV. However, but because of the mutation of the configuration of the virus following infection, a feature of HIV, an accurate vaccine has not yet been found. In addition, although many therapeutic medications for HIV have been developed, none completely cure HIV. Furthermore, current AIDS drugs (protease inhibitors, non-nucleoside reverse transcriptase inhibitors, nucleoside reverse transcriptase inhibitors, etc.) employ complex techniques. Long-term administration of these agents causes patients to suffer persistent adverse events, such as anemia, peripheral neuritis, pancreatitis, nausea, and headaches. Also, the possibility of long-term administration resulting in drug resistance cannot be ruled out. Yet another disadvantage of current treatment modalities is cost, in that current therapeutic medications for HIV are extremely expensive, often ranging between \$15,000 to \$20,000 per person per year, which necessarily limits patient access.

One type of agent that represents an effective alternative to current HIV treatment modalities is the delayed-type hypersensitivity (DTH) inducing agent, which type of agent has been researched as an immunomodulator that elicits immunological response in HIV patients by increasing the activity of the immune system cells in the body. Delayed-type hypersensitivity inducers are substances that induce Type 4 hypersensitivity when they come into contact with human skin, and they include trinitrobenzene sulfonic acid, picryl chloride (PC), 2,4-dinitrofluorobenzene (DNFB), and 1-chloro-2,4-dinitrobenzene (DNCB). Of these, DNCB has been widely used in the treatment of HIV and in immunological research, and the present invention focuses on DNCB as a DTH inducer in many embodiments, as described in greater detail below.

DNCB was discovered in Germany before World War II. Research conducted in the 1950s in the US demonstrated that DNCB is not carcinogenic. Later, in the 1970s, safety research was conducted in various types of animals. DNCB is generally known to be a powerful, delayed allergy-inducing skin irritant in humans, and is used in, among other things, immunological tests of skin diseases.

Research on DNCB therapy in HIV patients began slowly from the middle of the 1980s, and research on DNCB therapy in HIV patients was conducted in the first half of the

2

1990s, from which DNCB was claimed to be effective for treating HIV. However, this claim was not proved. In the latter half of the 1990s, the development of PCR analysis technology began to confirm the efficacy of DNCB in HIV patients. In addition, DNCB was also previously investigated as a possible treatment for cancer: tests were conducted in which DNCB was applied locally to induce a delayed allergic reaction and thereby utilize its immunity inducing capabilities. However, these findings have not been put to practical use. Furthermore, DNCB has been used in, among other things, the treatment of warts.

A method for using DNCB in HIV patients that has been employed in recent years has been to dissolve the DNCB in an acetone solvent and impregnate a gauze-like cloth with the resulting product and apply this to the skin. This topical preparation is then dried, covered and left to stand for several hours (typically at least 8 hours). This long application time means that an HIV patient would be restricted for at least 8 hours, a fairly long time, which would prevent that person from leading the same lifestyle as a healthy person.

There is considerable interest, therefore, in the development of a topical DTH inducing agent composition that could efficiently deliver an effective amount of a DTH inducing agent to a host in a short period of time.

Relevant Literature

References of interest include: Stricker et al. Dendritic cells and dinitrochlorobenzene (DNCB): A new treatment approach to AIDS. *Immunol Letters* 1991;29:191-196; Stricker et al. Pilot study of topical dinitrochlorobenzene (DNCB) in human immunodeficiency virus infection. *Immunol Letters* 1993;36:1-6; Stricker et al. Topical dinitrochlorobenzene in HIV disease. *J Am Acad Dermatol* 1993;28:796-797; Stricker et al. Clinical and immunologic evaluation of HIV-infected patients treated with dinitrochlorobenzene (DNCB). *J Am Acad Dermatol* 1994;31:462-466; Stricker R B, Goldberg B, Mills L B, Epstein W L. Improved results of delayed-type hypersensitivity skin testing in HIV-infected patients treated with topical dinitrochlorobenzene (DNCB). *J Am Acad Dermatol* 1995;33:608-611; Stricker & Goldberg. Safety of topical dinitrochlorobenzene. *Lancet* 1995;346:1293; Stricker et al. Improved results of delayed-type hypersensitivity skin testing in HIV-infected patients treated with topical dinitrochlorobenzene. *J Am Acad Dermatol* 1996;35:491-493; Stricker et al. Decrease in viral load associated with topical dinitrochlorobenzene therapy in HIV disease. *Res Virol* 1997;148:343-348; Traub et al. Topical immune modulation with dinitrochlorobenzene (DNCB) in HIV disease: A controlled trial from Brazil. *Dermatology* 1997;195:369-373; Stricker et al. Topical immune modulation (TIM): A novel approach to the immunotherapy of systemic disease. *Immunol Letters* 1997;59:145-150; Oracion et al. DNCB treatment of HIV-infected patients leads to beneficial immunologic outcomes, reduced viral load, and improved measures of quality-of-life. *J Invest Dermatol* 1998;110:476.

SUMMARY OF THE INVENTION

Topical patch preparations that contain a delayed-type hypersensitivity inducer, e.g., 1-dichloro-2,4-dinitrobenzene (DNCB), and methods for using the same are provided. The subject topical patch preparations are made up of an adhesive gel composition that is present on a support, where the adhesive gel composition includes the delayed-type hypersensitivity inducer, a water-soluble polymer gel, water and a water holding agent. In using the subject topical patch preparations, the topical patch preparations are applied to a

skin surface of a subject and maintained at the site of application for a period of time sufficient for an effective amount of the delayed-type hypersensitivity inducer to be administered to the subject, where this maintenance period typically does not exceed about 60 minutes. The subject invention finds use in a variety of applications where the administration of a delayed-type hypersensitivity inducer is desired, and is particularly suited for use in the treatment of HIV associated disease conditions, e.g., AIDS.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 provides a cross-sectional view of a topical patch preparation according to the invention.

FIGS. 2 and 3 provide schematic representations of the manufacturing process for topical patch preparations of the invention.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

Topical patch preparations that contain a delayed-type hypersensitivity inducer, e.g., 1-dichloro-2,4-dinitrobenzene (DNFB), and methods for using the same are provided. The subject topical patch preparations are made up of an adhesive gel composition that is present on a support, where the adhesive gel composition includes the delayed-type hypersensitivity inducer, a water-soluble polymer gel, water and a water holding agent. In using the subject topical patch preparations, the topical patch preparations are applied to a skin surface of a subject and maintained at the site of application for a period of time sufficient for an effective amount of the delayed-type hypersensitivity inducer to be administered to the subject, where this maintenance period typically does not exceed about 60 minutes. The subject invention finds use in a variety of applications where the administration of a delayed-type hypersensitivity inducer is desired, and is particularly suited for use in the treatment of HIV associated disease conditions, e.g., AIDS. In further describing the subject invention, the topical patch preparations are described first in greater detail, followed by a review of representative applications in which the subject topical patch preparations find use.

Before the subject invention is described further, it is to be understood that the invention is not limited to the particular embodiments of the invention described below, as variations of the particular embodiments may be made and still fall within the scope of the appended claims. It is also to be understood that the terminology employed is for the purpose of describing particular embodiments, and is not intended to be limiting. Instead, the scope of the present invention will be established by the appended claims.

In this specification and the appended claims, singular references include the plural, unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this invention belongs.

Topical Patch Preparations

As summarized above, the subject invention is directed to topical patch preparations of a delayed-type hypersensitivity inducer agent. The topical patch preparations of the subject invention are characterized by having an effective amount of the delayed type hypersensitivity inducer agent present in a gel adhesive base. FIG. 1 provides a representation of a topical patch preparation described according to the subject invention. As can be seen in FIG. 1, this representative topical patch preparation 10 contains a gel adhesive base 12

present on a support 14. Each of these components is now described in greater detail.

The gel adhesive base which serves as the delayed-type hypersensitivity inducer retaining layer, is made up of the delayed-type hypersensitivity inducer that is present in, e.g., dissolved in or dispersed in, and adhesive gel base. By "delayed-type hypersensitivity (DTH) inducers" is meant an immunomodulator that elicits immunological response in a subject, such as HIV patients, by increasing the activity of the immune system cells in the body. Delayed-type hypersensitivity inducers are substances that induce Type 4 hypersensitivity when they come into contact with human skin, and they include, but are not limited to: trinitrobenzene sulfonic acid, picryl chloride (PC), 2,4-dinitrofluorobenzene (DNFB), and 1-chloro-2,4-nitrobenzene (DNFB). In many embodiments, the delayed-type hypersensitivity inducer is DNFB.

The amount of DTH inducer that is present in the adhesive gel base is an amount sufficient to administer to a subject an effective amount of the agent when applied to a skin surface of the subject, as described in greater detail below. In many embodiments, the amount of DTH inducer present in the adhesive gel base ranges from about 0.01 to 10.0% (w/w), sometimes from about 0.05 to 10.0% (w/w), usually from about 0.1 to 5.0% (w/w) and more usually from about 0.2 to 3.0% (w/w).

The adhesive gel base that includes the DTH inducer, as described above, is made up of a water-soluble high molecular weight substance, water and a water retaining agent. In certain embodiments, the adhesive gel base may further include a cosolvent, e.g., an organic cosolvent. Each of these components is now described separately in greater detail.

Water-soluble high molecular weight substances of interest include water-soluble polymers, where polymers of interest include, but are not limited to: gelatin, starch, agar, mannan, alginic acid, polyacrylic acid, polyacrylate, dextrin, methylcellulose, sodium methylcellulose, hydroxypropylcellulose, sodium carboxymethylcellulose, cellulose gum, carboxyvinyl polymer, polyvinyl alcohol, polyvinylpyrrolidone, Arabia gum, acacia, tragacanth gum, karaya gum, and starch acrylate copolymer or other starch sodium acrylate graft copolymers. Metallic salts of these, as well as the products of cross-linking these by means of organic or inorganic cross-linking agents, are also of interest. These water-soluble polymers can be used to bring out the properties and characteristics of the other starting materials used in the adhesive gel composition, and in practice can be used alone or in combinations of 2 or more. The amount of water soluble high molecular weight substance(s) present in the adhesive gel base generally ranges from about 0.5 to 20, usually from about 2 to 20% (w/w).

While any convenient water may be employed as the water component, of interest are distilled water or ion-exchange water or the like, which is preferred in many embodiments of the subject invention. The amount of water present in the gel adhesive is sufficient to impart the desired physical properties to the gel adhesive, and to improve the swelling of the horny or keratinized layer of the skin to thereby improve the permeability or penetration of the DTH inducing agent(s), where the amount of water in the gel composition generally ranges from about 10 to 80%, usually from about 30 to 60% (w/w).

The water-retaining agent or water-holding agent of the subject adhesive gel compositions is any agent that is capable of at least diminishing the volatilization of water contained in the adhesive gel base so that the water content in the adhesive gel base is maintained at least a substantially

constant, if not constant, level during storage and use of the preparation. One or more water-retaining agents may be employed in the subject compositions, where the amount of water-retaining agent present in the adhesive gel base generally ranges from about 1 to 70%, more preferably 10 to 60% by weight. Examples of suitable water-retaining or water-holding agents include, but are not limited to: 1 or more types of polyvalent or polyhydric or sugars or alcohols, such as glycerin, sorbitol, propylene glycol, diethylene glycol, 1,3-butylene glycol, and ethylene glycol, and the like.

In addition, the subject gel base compositions may also include a cosolvent, where the cosolvent is generally an organic cosolvent. Examples of DNCB cosolvents of interest include, but are not limited to, n-methyl-2-pyrrolidone, crotonamiton, ethyl alcohol, methyl alcohol, polyethylene glycol (e.g., low molecular weight polyethylene glycol, such as PEG 600 or lower, e.g., 500, 400, 300, 200, 100 etc and blends thereof, and acetone, where n-methyl-2-pyrrolidone, polyethylene glycol and crotonamiton are of particular interest. The cosolvent may be made up of a simple component or be in combination of two or more components.

Furthermore, in addition to the aforementioned ingredients, various additives that are used in ordinary topical water-soluble patch preparations may also be suitably compounded as needed, including inorganic substances such as kaolin, bentonite, and titanium dioxide; preservatives such as parabens; anionic, cationic, and nonionic surfactants; metallic aluminum crosslinking agents such as aluminum chloride, dried aluminum hydroxide gel, and dihydroxyaluminum aminoacetate; oils such as jojoba oil and castor oil; chelating agents such as EDTA; pH regulators such as malic acid, tartaric acid, and diisopropanolamine; alcohols such as ethanol; moisture retaining agents such as hyaluronic acid, aloe extract, and urea; and other perfumes and coloring agents.

The pH of the gel base composition typically is one that lies in a physiologically acceptable range, where the pH typically ranges from about 4.0 to 7.0 and more typically ranges from about 4.0 to 6.0.

As mentioned above, the adhesive gel composition containing the one or more active ingredients is typically present on a support or backing. The support is generally made of a flexible material which is capable of fitting in the movement of human body and includes, for example, various non-woven fabrics, woven fabrics, spandex, flannel, or a laminate of these materials with polyethylene film, polyethylene glycol terephthalate film, polyvinyl chloride film, ethylene-vinyl acetate copolymer film, polyurethane film, and the like.

In addition to the adhesive gel composition and the support layer, the subject topical patches may also include a release film 16 on the surface of the gel layer opposite the backing that provides for protection of the gel layer from the environment. The release film may be any convenient material, where representative release films include polyesters, such as PET or PP, and the like.

In many embodiments, the patch is present in a sealed package. Generally, the sealed package is fabricated from a packaging material that includes a layer made out of a material capable of preventing passage of moisture, oxygen and other agents, i.e., the package includes in a moisture/oxygen barrier material. Any suitable barrier material may be employed, where barrier materials of interest include metallic layers, e.g., aluminum, where in many embodiments, the barrier layer is an aluminum layer. This barrier layer has a thickness sufficient to provide for the

barrier function, where the thickness typically ranges from about 5 to 15, usually from about 6 to 10 μm . In many embodiments, the package is a laminate of the barrier layer in combination with one or more additional layers, e.g., polymeric layers, paper layers, etc. A representative aluminum containing package that may be used with the subject patch preparations is sold by Dainippon Printing Co., Ltd. (Kyoto, Japan).

The topical patch preparations may be fabricated using any convenient protocol. One convenient protocol for fabrication of the subject patches includes preparing a gel adhesive paste through the uniform mixing of the aforementioned ingredients and then coating the paste onto the support, followed by cutting of the resultant product to the specified size to obtain the desired topical patch preparation. The resultant topical patch preparation is then heat-sealed, typically several sheets to a package, using a packaging material containing an aluminum layer, as described supra, to obtain the sealed topical patch. For a more detailed description of the fabrication protocol, see U.S. Pat. No. 5,827,529; the disclosure of which is herein incorporated by reference.

In a representative fabrication protocol, the base used in the present invention is produced by using a mixer to uniformly blend the aforementioned ingredients by means of any convenient protocol into a paste, which is then spread by means of a spreader onto a backing or support material. As indicated above, the support material may be, for example, paper, or a woven or nonwoven cloth made of PET or PP or some other polyester fiber. For protection, the surface thereof is then covered with a release film of a polyester such as PET or PP. These steps are illustrated in FIG. 2.

The resulting product is then cut to the specified size to obtain the desired topical patch preparation composition. The shape of the patch may vary, where representative shapes include square, rectangle, oval, circle, etc. The size of the patch may also vary, where in many embodiments the size ranges from about 1 to 200 cm^2 , and in many embodiments from about 10 to 100 cm^2 , usually from about 20 to 50 cm^2 , e.g., 25 cm^2 . The weight of the base in the final topical patch should be 300 to 1500 g/m^2 , and preferably 600 to 1000 g/m^2 . This water-soluble topical patch preparation is then packaged by means of a heat seal in a packaging material that includes a layer of aluminum to obtain the final product, as shown in FIG. 3.

It should be noted that the above manufacturing protocols are merely representative. Any convenient protocol that is capable of producing the subject topical patch preparations, as described above, may be employed.

50 Methods of Using Patch Preparations

The subject patch preparations find use in the topical delivery of DTH inducing agents, e.g., DNCB, to a host. By "topical delivery" is meant delivery via absorption through the skin. In using the subject topical patch preparations to topically administer a DTH inducing agent to the host, the topical preparation is applied to a skin surface and maintained at the site of application for a period of time sufficient for the desired amount of DTH inducing agent to be delivered to the host. In many embodiments, the period of time required to deliver the desired amount of agent is short, generally not exceeding about 60 minutes, usually not exceeding about 30 minutes and in many embodiments not exceeding about 15 minutes. However, the period of time during which the preparation is maintained at the application site is, in many embodiments, at least about 1 minute, usually at least about 3 minutes and more usually at least about 5 minutes.

11

therefore able to lead exactly the same lifestyle as a healthy person. In addition, concomitant use with other HIV therapeutic medications is also quite possible. Research has been conducted for some time into the adverse events of DNCB, and there have not been any reports to date of cases of life-threatening adverse events, such as carcinogenicity. Moreover, the DNCB water-soluble topical patch preparation of the present invention is only applied once a week, so treatment is possible at a cost of approximately \$300 per person per year, making it cheaper than other HIV therapeutic medications and making it possible to use it in developing countries as well.

It is evident from the above results and discussion that the subject invention provides for a number of advantages in the delivery of DTH inducing agents. The subject topical preparations are efficient and effective delivery vehicles for administration of a DTH inducing agent to a subject, and need only be applied for a short period of time in order to provide the agent administration. Furthermore, the subject topical patch preparations are 25° C. storage stable. The subject preparations represent a low cost way of treating many disease conditions, including AIDS. As such, the subject invention represents a significant contribution to the art.

All publications and patents cited in this specification are herein incorporated by reference as if each individual publication or patent were specifically and individually indicated to be incorporated by reference. The citation of any publication is for its disclosure prior to the filing date and should not be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it is readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

What is claimed is:

1. A topical patch preparation comprising:
 - (a) an adhesive gel composition having a pH ranging from about 4.0 to 7.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.01 to 10.0% (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 10 to 80% (w/w);
 - (iv) an ionic aluminum crosslinking agent; and
 - (v) a water retaining agent; and
 - (b) a support.
2. The topical patch preparation according to claim 1 wherein said DNCB is present in an amount ranging from about 0.1 to 5.0% (w/w).
3. The topical patch preparation according to claim 2 wherein said DNCB is present in an amount ranging from about 0.2 to 3.0% (w/w).
4. The topical patch preparation according to claim 1, wherein said water is present in an amount ranging from about 20 to 70% (w/w).
5. The topical patch preparation according to claim 4, wherein said water is present in an amount ranging from about 30 to 60% (w/w).
6. The topical patch preparation according to claim 1, wherein said pH ranges from about 4.0 to 6.0.
7. The topical patch preparation according to claim 6, wherein said adhesive gel composition further comprises an organic solvent.
8. The topical patch preparation according to claim 7, wherein said organic solvent is selected from the group

12

consisting of n-methyl-2-pyrrolidone, polyethylene glycol, and crotamiton and combinations thereof.

9. A topical patch preparation comprising:

- (a) an adhesive gel composition having a pH ranging from about 4.0 to 6.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.2 to 3.0% (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 30 to 60% (w/w);
 - (iv) a water retaining agent;
 - (v) an organic cosolvent selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotamiton and combinations thereof; and
 - (vi) a ionic aluminum crosslinking agent; and
- (b) a support.

10. A topical patch preparation comprising:

- (a) a release film;
- (b) an adhesive gel composition having a pH ranging from about 4.0 to 7.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.01 to 10.0% (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 10 to 80% (w/w);
 - (iv) a water retaining agent; and
 - (v) a ionic aluminum crosslinking agent; and
- (c) a support.

11. The topical patch preparation according to claim 10, wherein said DNCB is present in an amount ranging from about 0.1 to 5.0% (w/w).

12. The topical patch preparation according to claim 11, wherein said DNCB is present in an amount ranging from about 0.2 to 3.0% (w/w).

13. The topical patch preparation according to claim 10, wherein said water is present in an amount ranging from about 20 to 70% (w/w).

14. The topical patch preparation according to claim 13, wherein said water is present in an amount ranging from about 30 to 60% (w/w).

15. The topical patch preparation according to claim 10, wherein said pH ranges from about 4.0 to 6.0.

16. The topical patch preparation according to claim 15, wherein said adhesive gel composition further comprises an organic solvent.

17. The topical patch preparation according to claim 16, wherein said organic solvent is selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol, and crotamiton and combinations thereof.

18. A topical patch preparation comprising:

- (a) a release film;
- (b) an adhesive gel composition having a pH ranging from about 4.0 to 6.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.2 to 3.0% (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 30 to 60% (w/w);
 - (iv) a water retaining agent;
 - (v) an organic cosolvent selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotamiton and combinations thereof; and
 - (v) a ionic aluminum crosslinking agent; and
- (c) a support.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,526	02/21/2002	Jutaro Shudo	TEIK-004	8649
24353	7590	03/02/2004	EXAMINER	
BOZICEVIC, FIELD & FRANCIS LLP 200 MIDDLEFIELD RD SUITE 200 MENLO PARK, CA 94025			GHALI, ISIS A D	
			ART UNIT	PAPER NUMBER
			1615	

DATE MAILED: 03/02/2004

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 67 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 67 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.



Notice of Allowability

Application No.

10/080,526

Examiner

Isis Ghali

Applicant(s)

SHUDO ET AL.

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 11/26/2003.
2. ☒ The allowed claim(s) is/are 9-17 and 49-57.
3. ☒ The drawings filed on 21 February 2002 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material

5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date 02/25/2004.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

G S Kishore
Gollamudi S. Kishore, PhD
Primary Examiner
Group 1600

The receipt is acknowledged of applicant's amendment filed 11/26/2003.

Claims 8-36 have been canceled, and claims 41-57 have been added per applicant's amendment.

Claims 1-17, 37-57 are pending.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Bret Field on 02/25/2004.

The application has been amended as follows:

- (1) Cancel claims 1-8, 37-48.
- (2) In claim 9, line 7, the word "metallic" has been replaced by --- ionic ---.
- (3) In claim 17, line 11, the word "metallic" has been replaced by --- ionic ---.
- (4) In claim 49, line 9, the word "metallic" has been replaced by --- ionic ---.
- (5) In claim 57, line 12, the word "metallic" has been replaced by --- ionic ---.

Allowable Subject Matter

2. The following is an examiner's statement of reasons for allowance: the closest prior art does not teach or suggest topical patch comprising support; and an adhesive gel composition having pH 4.0-7.0 and comprising the active agent DNCB in the claimed amounts, water-soluble polymer gel, water in the claimed amount, water-retaining agent, and ionic aluminum cross linking agent that cross-links the gel composition.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

3. Claims 9-17, 49-57 are allowed.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1615

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

IG


Gollamudi S. Kishore, PhD
Primary Examiner
Group 1500

Interview Summary

Application No.

10/080,526

Applicant(s)

SHUDO ET AL.

Examiner

Isis Ghali

Art Unit

1615

All participants (applicant, applicant's representative, PTO personnel):

(1) Isis Ghali.

(3) _____.

(2) Mr. Bret Field.

(4) _____.

Date of Interview: 25 February 2005.

Type: a) ☒ Telephonic b) ☐ Video Conference

c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☒ No.

If Yes, brief description: _____.

Claim(s) discussed: Claims of record.

Identification of prior art discussed: None.


Agreement with respect to the claims f) ☒ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The examiner informed the attorney that claims 9-17 and 49-57 are in condition for allowance subjected to canceling claims 1-8 and 37-48; and changing the word "metallic" in claims 9, 17, 49 and 57 into ---- ionic ----. The attorney agreed and authorized the examiner to do the changes by "Examiner's Amendment".

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.


Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

VIA Express Mail

EV 333978812US

**RESPONSE &
AMENDMENT**

Address to:
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Attorney Docket	TEIK-004
First Named Inventor	Jutaro Shudo
Application Number	10/080,526
Filing Date	February 21, 2002
Group Art Unit	1615
Examiner Name	Isis Ghali
Title	Topical Patch Preparation
Paper No.	

Sir:

In response to the First Office Action dated September 23, 2003, please enter the following amendments:

AMENDMENTS

IN THE CLAIMS:

1. (Currently Amended) A topical patch preparation of a delayed-type hypersensitivity inducer, said preparation comprising:
an adhesive gel composition comprising a metallic aluminum crosslinking agent
and a delayed-type hypersensitivity inducer; and
a support.
2. (Original) The topical patch preparation according to Claim 1, wherein said delayed-type hypersensitivity inducer is 1-Chloro-2,4-Dinitrobenzene (DNCB).
3. (Original) The topical patch preparation according to Claim 2, wherein said DNCB is present in said adhesive gel composition in an amount ranging from about 0.01 to 10.0 % (w/w).
4. (Original) The topical patch preparation of Claim 1, wherein said adhesive gel composition comprises:
a water-soluble polymer gel;
water; and
a water retaining agent.
5. (Original) The topical patch preparation according to Claim 4, wherein said water is present in an amount ranging from about 10 to 80 % (w/w).
6. (Original) The topical patch preparation according to Claim 1, wherein said adhesive gel composition has a pH ranging from about 4.0 to 7.0.
7. (Original) The topical patch preparation according to Claim 1, wherein said adhesive gel composition further comprises an organic solvent.

8. (Original) The topical patch preparation according to Claim 7, wherein said organic solvent is selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotonamiton and combinations thereof.
9. (Currently Amended) A topical patch preparation comprising:
- (a) an adhesive gel composition having a pH ranging from about 4.0 to 7.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.01 to 10.0 % (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 10 to 80 % (w/w); and
 - (iv) a metallic aluminum crosslinking agent; and
 - (v) a water retaining agent; and
 - (b) a support.
10. (Original) The topical patch preparation according to Claim 9, wherein said DNCB is present in an amount ranging from about 0.1 to 5.0 % (w/w).
11. (Original) The topical patch preparation according to Claim 10, wherein said DNCB is present in an amount ranging from about 0.2 to 3.0% (w/w).
12. (Original) The topical patch preparation according to Claim 9, wherein said water is present in an amount ranging from about 20 to 70% (w/w).
13. (Original) The topical patch preparation according to Claim 12, wherein said water is present in an amount ranging from about 30 to 60 % (w/w).
14. (Original) The topical patch preparation according to Claim 9, wherein said pH ranges from about 4.0 to 6.0.
15. (Original) The topical patch preparation according to Claim 14, wherein said adhesive gel composition further comprises an organic solvent.

16. (Original) The topical patch preparation according to Claim 15, wherein said organic solvent is selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol, and crotamiton and combinations thereof.

17. (Currently Amended) A topical patch preparation comprising:

(a) an adhesive gel composition having a pH ranging from about 4.0 to 6.0 and comprising:

- (i) DNCB in an amount ranging from about 0.2 to 3.0 % (w/w);
- (ii) a water-soluble polymer gel;
- (iii) water in an amount ranging from about 30 to 60 % (w/w);
- (iv) a water retaining agent; and
- (v) an organic cosolvent selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotamiton and combinations thereof; and

(vi) a metallic aluminum crosslinking agent; and

(b) a support.

Claims 18 to 36 (Cancelled).

37. (Currently Amended) A kit for use in transdermal delivery of a delayed-type hypersensitivity inducer to a subject in need thereof, said kit comprising:

(a) a topical patch preparation comprising:

(i) an adhesive gel composition comprising an effective amount of a delayed-type hypersensitivity inducer and a metallic aluminum crosslinking agent; and

(ii) a support; and

(b) instructions for using said preparation.

38. (Original) The kit according to Claim 37, wherein said kit comprises a plurality of said topical patch preparations.

39. (Original) The kit according to Claim 38, wherein said plurality of topical patch preparations are present in separate containers.
40. (Original) The kit according to Claim 39, wherein said separate containers are sealed pouches.
41. (New) A topical patch preparation of a delayed-type hypersensitivity inducer, said preparation comprising:
- a release film;
 - an adhesive gel composition comprising a delayed-type hypersensitivity inducer and a metallic aluminum crosslinking agent; and
 - a support.
42. (New) The topical patch preparation according to Claim 41, wherein said delayed-type hypersensitivity inducer is 1-Chloro-2,4-Dinitrobenzene (DNCB).
43. (New) The topical patch preparation according to Claim 42, wherein said DNCB is present in said adhesive gel composition in an amount ranging from about 0.01 to 10.0 % (w/w).
44. (New) The topical patch preparation of Claim 41, wherein said adhesive gel composition comprises:
- a water-soluble polymer gel;
 - water; and
 - a water retaining agent.
45. (New) The topical patch preparation according to Claim 44, wherein said water is present in an amount ranging from about 10 to 80 % (w/w).

46. (New) The topical patch preparation according to Claim 41, wherein said adhesive gel composition has a pH ranging from about 4.0 to 7.0.
47. (New) The topical patch preparation according to Claim 41, wherein said adhesive gel composition further comprises an organic solvent.
48. (New) The topical patch preparation according to Claim 47, wherein said organic solvent is selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotamiton and combinations thereof.
49. (New) A topical patch preparation comprising:
- (a) a release film;
 - (b) an adhesive gel composition having a pH ranging from about 4.0 to 7.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.01 to 10.0 % (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 10 to 80 % (w/w);
 - (iv) a water retaining agent; and
 - (v) a metallic aluminum crosslinking agent; and
 - (c) a support.
50. (New) The topical patch preparation according to Claim 49, wherein said DNCB is present in an amount ranging from about 0.1 to 5.0 % (w/w).
51. (New) The topical patch preparation according to Claim 50, wherein said DNCB is present in an amount ranging from about 0.2 to 3.0% (w/w).
52. (New) The topical patch preparation according to Claim 49, wherein said water is present in an amount ranging from about 20 to 70% (w/w).

53. (New) The topical patch preparation according to Claim 52, wherein said water is present in an amount ranging from about 30 to 60 % (w/w).

54. (New) The topical patch preparation according to Claim 49, wherein said pH ranges from about 4.0 to 6.0.

55. (New) The topical patch preparation according to Claim 54, wherein said adhesive gel composition further comprises an organic solvent.

56. (New) The topical patch preparation according to Claim 55, wherein said organic solvent is selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol, and crotamiton and combinations thereof.

57. (New) A topical patch preparation comprising:

- (a) a release film;
- (b) an adhesive gel composition having a pH ranging from about 4.0 to 6.0 and comprising:
 - (i) DNCB in an amount ranging from about 0.2 to 3.0 % (w/w);
 - (ii) a water-soluble polymer gel;
 - (iii) water in an amount ranging from about 30 to 60 % (w/w);
 - (iv) a water retaining agent;
 - (v) an organic cosolvent selected from the group consisting of n-methyl-2-pyrrolidone, polyethylene glycol and crotamiton and combinations thereof; and
 - (v) a metallic aluminum crosslinking agent; and
- (c) a support.

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-24 and 37-40, as well as newly added Claims 41 to 57, the only claims pending and under examination at this time following entry of the above amendments.

The undersigned thanks the Examiner for the helpful personal interview held on November 5, 2003. During the interview of November 5, 2003, the claims were discussed with respect to the cited Hopp reference.

Claims 1, 9, 17 and 37 have been amended to recite that the adhesive gel compositions include a metallic aluminum crosslinking agent, support for this amendment being found in the specification at page 7, lines 14 to 16, as well as Tabel 1 of the working exemplification. New Claims 41-57 are analogous to Claims 1 to 17, but include the specific additional element of a release film, which element finds support in the specification at page 7, lines 29 ff. As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

Claims 1-4, 7, 18-22 and 24 have been rejected under 35 U.S.C. § 102 (e) as being anticipated by US 5,846,599 ('599).

As explained below, the '599 patent fails to teach or suggest an adhesive patch as claimed, since the adhesive patch claimed is one that includes a metallic aluminum crosslinking agent, which agent imparts the adhesive properties to the claimed patch composition such that the patch is self-adhesive.

The '599 patent teaches a skin patch for delivery of a contactant to human skin and specifically the '599 patent teaches a supply of contactant that is enclosed in a shroud (see for example col. 5, lines 17-20; Figs. 1-10). However, the '599 patent

teaches that in order to provide adhesiveness for the skin patch, an adhesive coated flange surrounds the shroud and enables the skin patch to be adhered to the skin (col. 5, lines 39-56). Further to this point, the '599 patent explicitly states: "The outer surface or undersurface of the adhesive flange 11 is coated with an adhesive that assures persistence of the device on the skin" (col. 5, lines 49-51). The '599 patent describes various exemplary materials that may be used for the adhesive coated flange (col. 5, lines 43-48), as well as adhesives useable about the flange to provide the needed adhesive property (col. 5, lines 52-56). As such, the '599 patent fails to teach or suggest a gel composition component as claimed, which is itself an adhesive gel composition.

Furthermore, the claimed gel composition must include a metallic aluminum crosslinking agent. This crosslinking agent imparts the self-adhesive properties to the gel component. The '599 fails to teach or suggest such a crosslinking agent.

Accordingly, for at least the reasons provided above, the '599 patent does not anticipate 1-4, 7, 18-22 and 24 and this rejection under 35 U.S.C. § 102 (e) may be withdrawn.

Claim 5 has been rejected under 35 U.S.C. § 103(a) over the '599 reference, for the asserted reason that the only difference between the claimed invention and the disclosure of the '599 reference is that the claimed invention specifies a particular water amount, which is assertedly obvious. However, as demonstrated above, the '599 patent fails to teach or suggest a topical patch composition as now claimed, because the '599 patent teaches the criticality of having an adhesive flange, and fails to teach a self-adhesive gel composition, much less one that specifically includes a metallic aluminum cross linking agent. Accordingly, Claim 5 is not obvious over the '599 disclosure and this rejection may be withdrawn.

Next, Claims 5, 6, 8-17 and 23 have been rejected under 35 U.S.C. § 103(a) over the '599 patent in view of U.S. Patent No. 5,891,920. As the '920 reference has been cited solely to make up for features such as pH and organic solvent, it fails to make up

the above described fundamental deficiency in the '599 patent. Accordingly, the combined teachings of the '599 patent in view of the '920 patent fail to render Claims 5, 6, 8-17 and 23 obvious and this rejection may be withdrawn.

Finally, Claims 37-40 have been rejected under 35 U.S.C. § 103(a) over the '599 patent in view of U.S. Patent No. 5,476,664. As the '664 reference has been cited solely to teach a kit that includes a plurality of patches, it fails to make up the fundamental deficiency in the '599 patent. Accordingly, the combined teachings of the '599 patent in view of the '664 patent fail to render Claims 37-40 obvious and this rejection may be withdrawn.

CONCLUSION

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

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Date: 11.26.03

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